IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

ELI LILLY AND COMPANY, Plaintiff, v. TEVA PARENTERAL MEDICINES, INC., APP PHARMACEUTICALS, LLC, PLIVA HRVATSKA D.O.O., TEVA PHARMACEUTICALS USA, INC., and BARR LABORATORIES, INC., Defendants.	)	Civil Action No. 1:10-cv-01376-TWP-DKL

PLAINTIFF ELI LILLY AND COMPANY'S OPENING POST-TRIAL BRIEF

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Few if any of the facts regarding infringement of Plaintiff Eli Lilly and Company's ("Lilly's") U.S. Patent No. 7,772,209 ("the '209 patent") are contested. The only dispute is whether physicians will "administer" folic acid as required by the asserted claims. The evidence is overwhelming that they will. As Plaintiffs' expert Dr. Chabner explained, the ordinary meaning of "administer" encompasses the way oncologists treat patients: they direct the treatment and cause it to be carried out, even if someone else physically puts a substance into the patient's body. ECF 409 ("Tr.") 82-84, 86, 125-26. Moreover, the patent uses the term the same way. Defendants' own expert Dr. Schulz conceded that "administer" is used by oncologists to describe instructing patients to take oral medication, and that the '209 patent does not redefine it to have a narrower meaning. Tr. 228-29, 232-34.

The question before the Court is whether a doctor using the Defendants' pemetrexed products would be a direct infringer of claims 9, 10, 12, 14, 15, 18, 19, and 21 of the '209 patent.[1] Lilly established that they would for three separate and independent reasons: (1) doctors will literally infringe, (2) doctors will infringe under the doctrine of equivalents, and (3) doctors will infringe because they direct or control the administration of folic acid.

Because physicians who use Defendants' products will directly infringe, Defendants will be liable for both inducing and contributing to infringement. 35 U.S.C. § 271(b), (c). As to inducement, the evidence established that Defendants' labeling will induce physicians to infringe Lilly's claims because it encourages doctors to practice every step of Lilly's claims. As to contribution, the evidence established that Defendants' products are especially made for use in Lilly's patented method and have no substantial non-infringing uses, and the remaining requirements for contributory infringement are met. Tr. 125; *see also* 35 U.S.C. § 271(c).

[1] The parties agree that for purposes of this litigation, Defendants' product labeling can be treated as identical to the current product labeling for ALIMTA®. ECF No. 358; TX 3017, 3018.

Indeed, Defendants offered no defense to contributory infringement other than that there will be no direct infringer—which means that if the Court finds for Lilly on any theory of direct infringement, Defendants have effectively conceded liability for contributory infringement.

In response, Defendants offered at trial a series of red herrings that only serve to confuse the issue before the Court, such as:

1. *Patients obtain and swallow folic acid pills so there can never be a single actor practicing Lilly's claims.* Defendants argued that the "single actor" rule precludes a finding of literal infringement because, even to the extent oncologists "administer" folic acid pills by instructing patients to take them, patients must still obtain those pills from a pharmacy and ingest them. Defendants' argument relies on the false premise that Lilly must show that doctors act in isolation in administering folic acid without any participation from the patient. The law makes clear, however, that the relevant question is *not* whether some response or cooperation from another person is needed for the purposes of the claim to be achieved; rather, *it is whether one single actor—the physician—carries out each expressly claimed step*. In other words, the question is whether the actions that the doctor takes satisfy the administration requirement. And the evidence showed that they do.

2. *Defendants' product labeling does not expressly require verification that patients have taken folic acid.* Defendants also argued that their product labeling does not expressly state that oncologists must verify that their patients have taken folic acid before providing pemetrexed. Whether it does or not is beside the point, however, as verification is not required for literal infringement. And in any event, the question under the law *is what the label induces physicians to do*, not just what it spells out expressly. Here, the evidence showed that the labeling not only expressly requires instructing patients to take folic acid and counseling them on the critical

importance of doing so, but it also, by its emphasis on the importance of folic acid supplementation and the dangers of failing to properly supplement before pemetrexed is provided, induces physicians to confirm that their patients have taken folic acid as directed, at a minimum by asking whether their patients have taken it.

3. *Lilly's doctrine of equivalents argument requires finding that the conduct of one person is equivalent to the conduct of two people.* The evidence showed that even if physicians do not literally infringe the folic acid administration limitations, the physician's conduct is equivalent to "administering" under Defendants' construction of the term. Defendants responded with another red herring, which is a variant of their "single actor" argument about literal infringement: the idea that the conduct of two people cannot be equivalent to the conduct of one single actor. Tr. 70. That argument makes the wrong comparison. The question under the doctrine of equivalents is whether *what the doctor actually does is equivalent to what is literally claimed*. To resolve that question, the Court looks to what conduct constitutes literal infringement, and then asks whether what the doctor actually does is insubstantially different from an act that literally falls within the scope of the claim.

Here, both sides agree that oncologists dropping folic acid pills into their patients' mouths would be "administering" folic acid, and if they did so, there would be infringement of Lilly's claims by a single actor. The evidence showed that what doctors actually do is equivalent to this: they instruct patients to take folic acid, impress upon them the importance of the folic acid, and verify that the patients have taken it before giving pemetrexed, which results in their patients receiving folate supplementation just as surely as if the doctors had put the pills on the patients' tongues. That means there is infringement under the doctrine of equivalents *by the doctor*.

4. *Patients might lie about having taken folic acid.* Defendants emphasized that physicians cannot ensure with 100% certainty that every patient has taken folic acid as directed—as Defendants' counsel baldly put it, "Maybe they are lying to the doctor." Tr. 74. This hypothetical possibility is beside the point because Lilly need not demonstrate infringement as to every single patient. Defendants infringe, rather, if their label would induce *even one* physician to infringe either literally or under the doctrine of equivalents—and the evidence established that in at least the vast majority (if not all) cases when physicians administer pemetrexed, patients have taken folic acid. The fact that some—heretofore unknown—theoretical sliver of patients might be lying does not defeat a finding of infringement.

The Court should not be distracted by Defendants' diversions. They are liable for infringement on multiple theories, and judgment should be entered for Lilly, including an order resetting the approval date of Defendants' ANDAs to no earlier than the date the patent expires. 35 U.S.C. § 271(e)(4); *Sunovion Pharms., Inc. v. Teva Pharms. USA, Inc.*, 731 F.3d 1271, 1278-79 (Fed. Cir. 2013).

I. PHYSICIANS WILL LITERALLY INFRINGE THE '209 PATENT

The sole disputed issue regarding literal infringement is whether physicians "administer" folic acid. Every other limitation of the claims is undisputedly met. Doctors (or other healthcare professionals at their direction) administer vitamin B_{12} and pemetrexed according to the specific requirements of the asserted claims. Dr. Chabner walked the Court through the asserted claims on a limitation-by-limitation basis, Tr. 84-91, and testified in detail about Defendants' labeling. Tr. 91-110. Comparing the claims to the labeling, Dr. Chabner then testified that use of Defendants' products would meet: (1) each of the claimed folic acid dose and schedule limitations, Tr. 115-16; (2) each of the claimed vitamin B_{12} dose and schedule limitations, Tr. 116-18; (3) the requirements in claim 12 of administering folic acid and vitamin B_{12} prior to the

first administration of pemetrexed, Tr. 122; and (4) each of the "effective amount" limitations of claims 9 and 10, Tr. 119-23. And as to the folic acid limitation, there is no dispute that patients receive folic acid according to the claimed regimen. Tr. 102-03, 115-16, 124 (Chabner); Tr. 240-48 (Schulz). The only debate is about what "administer" means, and thus *who* administers the folic acid.

The evidence showed that the physician "administers" folic acid "to a patient," as the claims of the patent require. *E.g.*, TX 1, claim 12. The patent itself, the file history, the ALIMTA® product labeling, and both parties' experts use the term "administer" to refer to prescribing the medication or instructing the patient to take it and thereby causing the patient to receive it. Tr. 83-86, 96, 101, 103-06, 125, 132, 233, 256-57, 261-64; TX 1, 201, 3018.

A. The Court Should Adopt Lilly's Construction of "Administer"

A claim term is given its "ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012) (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc)); ECF No. 115 (Entry on Claim Construction). The ordinary and customary meaning of a claim term governs unless one of two narrow exceptions applies: the patentee (1) has expressly redefined the term; or (2) has clearly disavowed some portion of its full scope. *See Thorner*, 669 F.3d at 1367-68. Defendants have not even argued that either exception applies here, and thus the ordinary and customary meaning controls.

1. The Ordinary and Customary Meaning of "Administer" in Oncology Includes a Physician Directing a Patient's Treatment Regimen

a. The evidence established the term "administering," as used by oncologists, encompasses a variety of ways oncologists can treat a patient. To be sure, they can physically

put a drug into a patient; Dr. Chabner administered intravenous infusions in this way early in his career. Tr. 82. Oncologists can also write orders that are then carried out by other healthcare professionals, such as by the specialist infusion nurses who typically infuse intravenous cancer chemotherapy. Tr. 82-83, 136-38. Oncologists can also treat the patient by administering oral medications, which is typically done by prescribing a pill or instructing a patient to take it. Tr. 83-84, 86, 125-26, 194, 232-33. All of these different ways that physicians treat patients with drugs have a common core: the physician directs a treatment and causes the patient to receive it. As the evidence showed, that is the ordinary and customary meaning of "administer" in oncology. Tr. 82-84, 86, 125-26. It is of course true that the ultimate purpose of administration is for the drug to be in the patient so it can have its desired effects; who puts it in the patient, however, is of no consequence. Tr. 133.

b. The physician prescribing information (or label) for ALIMTA®, which is "directed to the physician," Tr. 93, is extrinsic evidence of the ordinary meaning of the term "administer" to oncologists and shows that, contrary to Defendants' assertions, it includes instructing a patient to take an oral medication. The prescribing information instructs oncologists to "*[a]dminister* dexamethasone 4 mg *by mouth* twice daily." TX 3018, at 2 (emphases added); Tr. 105. As Dr. Chabner and Dr. Schulz agreed, dexamethasone is given orally as a pill. Tr. 103-05, 233. An oncologist would not understand the label to be directing that she physically place dexamethasone pills into the patient's mouth twice a day for several days. Tr. 105-06, 233. Rather, as both Dr. Chabner and Dr. Schulz testified, an oncologist would understand "[a]dminister dexamethasone" to mean "prescribe dexamethasone to your patients." Tr. 233 (Schulz); *see* Tr. 106 (Chabner). And Dr. Schulz testified that he in fact administers dexamethasone in precisely this way. Tr. 232.

The label's use of "administer" to mean prescribing or instructing patients to take oral dexamethasone is not an idiosyncratic usage; Dr. Schulz has used the term exactly the same way. In his January 2013 expert report in this case, Dr. Schulz wrote that "*Lilly administered dexamethasone* along with pemetrexed, folic acid, and vitamin B_{12}" in its clinical trials for ALIMTA®. Tr. 262 (emphasis added). Of course, "Lilly" itself did not put dexamethasone pills on or in a patient's body, nor did the physicians working on the relevant clinical trial physically put dexamethasone pills into patients' mouths. Tr. 263. Rather, as Dr. Schulz testified, his statement that "Lilly administered dexamethasone" referred to Lilly's role, as the sponsor of the clinical trial, in issuing directions that patients should take dexamethasone pills. Tr. 263-64. Dr. Schulz also conceded that this meaning of "administered"—*i.e.*, instructing patients to take medication—was an appropriate use of the term in the field of oncology. Tr. 264.

Other aspects of the label also support Lilly's position regarding the ordinary meaning of "administer." The "Dosage and *Administration*" section of the labeling tells the oncologist how to administer the pemetrexed regimen to the patient. TX 3018, at 2 (emphasis added); Tr. 101-02. Among other things, it tells the physician to administer folic acid by "instructing patients to initiate folic acid, 400 micrograms to 1,000 micrograms orally." Tr. 101; *see also* TX 3018, at 2. Thus, the label shows, and oncologists understand, that instructing a patient to take folic acid is "part of the *administration* of this regimen." Tr. 103 (emphasis added).

c. The testimony of Defendants' own experts, as well as Defendants' own briefing, also support Lilly's position. Although Dr. Schulz provided a conclusory opinion that "administer" means "putting a drug on or in a patient's body," there is simply no evidence that the term should be limited *only* to this act, and the rest of his testimony contradicts that view. Indeed, he admitted that oncologists use the term "administer" more broadly than his definition.

Tr. 228-29. He even conceded that "administer" could encompass a physician giving a drug to a patient that the patient would ingest. Tr. 206.[2]

In fact, when not testifying in support of a position in litigation, Dr. Schulz himself has used "administer" in his own scientific publication to mean prescribing an oral medication and instructing the patient to take it—exactly Lilly's position in this case and directly contrary to the construction Defendants advance. In an article in the journal *Lung Cancer*, Dr. Schulz described a clinical study in which patients were prescribed an oral chemotherapy drug. Tr. 256. After being instructed to take the medication by a healthcare professional, the patients swallowed the pills themselves. Tr. 256-57. The article explained that the drug "was administered," *id.*, and Dr. Schulz agreed that it was the healthcare provider in this study who "administered" the drug, even though the patients were the ones who physically ingested the pills. Tr. 257. Dr. Schulz's usage of "administer" is flatly inconsistent with his testimony and is persuasive extrinsic evidence of the term's ordinary meaning.

Another of Defendants' experts, Dr. Ralph Green—who testified at the validity trial before this Court in 2013—has also used "administer" to mean "prescribe." Dr. Green testified that when treating patients with a folate deficiency, his "approach would be *to administer folic acid by prescription*." Green Dep. Tr. 16:12-25 (emphasis added). Dr. Green's testimony that a doctor may administer folic acid "by prescription," rather than by putting folic acid directly into the patient's body, is consistent only with Lilly's proposed construction, not Defendants'.

Defendants themselves have acknowledged that "administer" is used in oncology

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[2] Specifically, Dr. Schulz testified that "administering" included "directly supervising [patients'] ingesting" a drug. Tr. 206. By this, he apparently meant that a physician would be "administering" a drug if she instructed a patient to take a pill and then watched the patient do so, but would not be "administering" if she instructed the patient to take a pill and the patient took the pill at home. Dr. Schulz provided no evidence to support this illogical distinction.

consistent with Lilly's construction. In their briefing in a case about an earlier patent covering pemetrexed, Defendants (represented by the same counsel as here) told the court that "[t]he physician prescribing information for ALIMTA® requires that *physicians co-administer* ALIMTA® with folic acid and vitamin B_{12} to reduce the toxicity of ALIMTA®." Defendants' Proposed Findings of Fact and Conclusions of Law at 8 (¶ 10), *Eli Lilly & Co. v. Teva Parenteral Meds. Inc.*, No. 1:08-cv-00335-GMS (D. Del. Oct. 5, 2010) (No. 88-12) (emphasis added) (filed in this case as ECF No. 369-7). Defendants thus agreed that the label directs "physicians" to administer the pemetrexed, the vitamin B_{12}, *and* the folic acid—and the label tells physicians to do so by instructing patients to take oral folic acid. That is entirely consistent with Lilly's position here and inconsistent with Defendants' position that "administration" is limited to the physical act of putting a substance into a patient.

In light of this evidence, there can be little doubt that the ordinary meaning of "administering" in oncology is directing a medical treatment and causing the patient to receive it. That can include physically putting the drug on or in the patient, but it plainly is not limited *only* to that physical act. To the contrary, "administering" includes precisely what Defendants' labeling here tells oncologists to do: instructing their cancer patients to take a particular dose of folic acid, leading the patients to do so. Tr. 86, 96-99, 110-12, 132-33.

2. The '209 Patent Uses "Administer" According To Its Ordinary and Customary Meaning

The evidence also established that the meaning of the term "administer" in the claims of the '209 patent is the same as the ordinary and customary meaning in oncology. The use of the term in the specification and claims is entirely consistent with its ordinary meaning, and Defendants do not even attempt to argue that the patent has redefined the term or clearly disavowed its full scope. *Thorner*, 669 F.3d at 1365. Indeed, Dr. Schulz conceded that

"[t]here's no specific definition in the patent of the term 'administer.'" Tr. 229. Dr. Chabner, too, testified that the '209 patent's claims, specification, and prosecution history all consistently use the term "administer" to include instructing a patient to take folic acid pills. Tr. 84.

a. *The Claims*. "[T]he claims themselves provide substantial guidance as to the meaning of particular claim terms." *Phillips*, 415 F.3d at 1314.

Claim 12, which is representative of the asserted claims, is directed to an "improved method for administering pemetrexed disodium to a patient." TX 1, claim 12. The body of the claim sets out three steps for the method of "administering pemetrexed," two of which have nothing to do with physically putting pemetrexed into the patient's body. Rather, they are about vitamin pretreatment. It cannot be, therefore, that "administering" is limited only to physically putting a substance into a patient. Moreover, the claim recites "administering pemetrexed disodium *to a patient*." *Id.* (emphasis added). The patient is the recipient of the medical treatment described in the claim, which is provided by a physician. The claim, therefore, is *directed to the physician* and is instructing her on what to do when treating her patient with pemetrexed. And as to folic acid, the person of ordinary skill would understand that the claim directs physicians to instruct patients to take folic acid, not to physically deliver it to their body. Tr. 85, 130-31.

Claim 21 also illustrates that the '209 patent's use of the term "administer" is consistent with its ordinary and customary meaning. The claim requires repeatedly giving vitamin B_{12} to the patient every few weeks "until administration of pemetrexed disodium is discontinued." TX 1, col. 12, ll. 26-27. If, as Defendants posit, "administration" of pemetrexed meant physically putting pemetrexed in the patient's body, claim 21 would make no sense as worded. It takes ten minutes to physically infuse pemetrexed into a patient, and then the needle is

removed and the physical infusion is "discontinued." TX 3018 at 2. Obviously, one cannot repeatedly give vitamin B_{12} every few weeks during these few minutes. Rather, claim 21 is talking about repeating vitamin B_{12} administration until the pemetrexed treatment that the physician directs and causes to occur is discontinued.

b. *The Specification*. Apart from the claim language, the patent's specification "is the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Like its claims, the '209 patent's specification also uses "administer" according to its ordinary and customary meaning. For example, in describing a "Method of Administration" for a clinical study involving pemetrexed and vitamin pretreatment, the specification states that "[f]olic acid will be supplied" to patients in the study, and that "patients should take oral folic acid daily." TX 1, col. 9, ll. 4-15. The clear import of this passage is that "administration" does not mean putting folic acid directly in the patients' mouths, but rather supplying oral folic acid pills to patients and instructing them to take them.[3]

c. *The Prosecution History*. A patent's publicly available prosecution history "provides evidence of how the [Patent Office] and the inventor understood the patent" and should be considered in construing a disputed claim. *See Phillips*, 415 F.3d at 1317. Here, the prosecution history also confirms that "administer" has its ordinary and customary meaning.

During prosecution, Lilly told the Patent Office that the claims cover the regimen in the ALIMTA® prescribing information. Quoting from the physician prescribing information, Lilly

[3] As discussed in Lilly's pre-trial brief, ECF No. 369 at 14-16, both the specification and prosecution history also support the ordinary meaning of "administer" by equating "administer" with "treat." *See* TX 1, col. 4, ll. 14-27; *id.* col. 6, ll. 22-27; TX 201, at AV00000449. The specification also uses the term "administer" to refer to providing folic acid-enriched water to mice, where the mice then drink the water. TX 1, col. 8, ll. 12-15. No person of ordinary skill would say that the mice therefore "administer" the folic acid to themselves. Tr. 132.

pointed out that according to this labeling, "[p]atients treated with ALIMTA must be instructed to take folic acid." TX 201, at AV00000454. The relevance of the prescribing information was the clinical toxicity data it reported, which Lilly argued were unexpected. *Id.* at AV00000455. And in order to be relevant, the data had to be from use of the invention recited in the claims. *See, e.g.*, *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003). Thus, when Lilly submitted its prescribing information to the Patent Office, it was telling the Examiner and the public that its claims cover the regimen described in that labeling—a regimen that included the physician instructing the patient to take oral folic acid.

* * *

In sum, the '209 patent's claims, specification, and prosecution history all use the term "administer" according to its ordinary and customary meaning—directing a patient's treatment regimen and thus causing the patient to receive the treatment.[4]

3. The Cases Cited by Defendants Do Not Inform the Ordinary Meaning of "Administer" in the Context of the '209 Patent

In support of their narrow construction of "administer," Defendants have cited cases in which other courts have construed the term in the context of other patents. *See* ECF No. 361 at 11, 14; Tr. 41. The Court should reject this attempted "construction by proxy."

First, it is hornbook law that claim construction is properly conducted based on the text and prosecution history *of the patent being construed*, not based on how courts have construed other unrelated patents (to say nothing of other fields). *e.Digital Corp. v. Futurewei Techs., Inc.*,

[4] Defendants point to a few instances where they say "administer" is used in a more narrow sense. Tr. 194-98, 203-05. But that has no bearing on the relevant question of whether its meaning is *limited* to physically putting into the patient. And even if Defendants were correct that the patent at times used "administer" more narrowly, the result is the same, as the Federal Circuit has repeatedly explained that the "varied use of a disputed term in the written description attests to the breadth of a term rather than providing a limiting definition." *Anchor Wall Sys., Inc. v. Rockwood Retaining Walls, Inc.*, 340 F.3d 1298, 1308 (Fed. Cir. 2003); *see also Prima Tek II, L.L.C. v. Polypap, S.A.R.L.*, 318 F.3d 1143, 1151 (Fed. Cir. 2003) (same).

772 F.3d 723, 727 (Fed. Cir. 2014) ("[C]laims of unrelated patents must be construed separately."); *Medrad, Inc. v. MRI Devices Corp.*, 401 F.3d 1313, 1318 (Fed. Cir. 2005) ("A particular term used in one patent need not have the same meaning when used in an entirely separate patent, particularly one involving different technology."). The relevant question here is how "administer" is used in the '209 patent in light of the evidence of its ordinary meaning in oncology and the '209 patent's claims, specification, and prosecution history. Looking to other cases about other patents based on other records does not aid this analysis.[5]

Second, as Defendants' counsel acknowledged in his opening, Tr. 57, plenty of cases support Lilly's interpretation of "administer." *See, e.g.*, *Pozen Inc. v. Par Pharm., Inc.*, 719 F. Supp. 2d 718 (E.D. Tex. 2010); *Janssen Prods., L.P. v. Lupin Ltd.*, No. 10-cv-05954(WHW), 2013 U.S. Dist. LEXIS 189016 (D.N.J. Jan. 7, 2014); *Shire LLC v. Amneal Pharm., LLC*, No. 11-3781(SRC), 2013 U.S. Dist. LEXIS 111773 (D.N.J. Aug. 8, 2013). While Defendants asserted at trial that the "closest" case is *Abbott Biotech. Ltd. v. Centocor Ortho Biotech, Inc.*, No. 09-40089-FDS, 2011 WL 3566964 (D. Mass. Aug. 12, 2011), left unsaid is why *Abbott* is somehow "closest." Tr. 57. In reality, it does nothing to resolve this case. Its statement that prescribing is distinct from administering—i.e., the entire reason that Defendants cite the case—was not disputed between the parties, and the court disposed of that issue in a mere three sentences. *Abbott*, 2011 WL 3566964, at *1, *6. Why the issue was not disputed is not disclosed in the opinion, but, obviously, a party's decision not to contest an issue is no evidence at all regarding how the court would have ruled had the distinction been an actual issue in

[5] Defendants' citation to Lilly's amicus brief in the Supreme Court in *Limelight* is similarly flawed. Not only was Lilly merely reciting arguments that others had made, not agreeing with those arguments, but Lilly's statements were not in the context of oncology, pemetrexed, or the '209 patent, making their relevance to the present dispute tangential to say the least and not proper extrinsic evidence of how the term should be construed in the '209 patent. Tr. 30.

contention. By contrast, in the cases Lilly cites, one party had expressly argued that "administer" should be construed to mean "the treating professional must physically deliver the pharmaceutical into the patient's mouth," and the courts rejected that construction. *E.g.*, *Shire*, 2013 U.S. Dist. LEXIS 111773, at *54.

For these reasons, Defendants' cases do not bear on the relevant question here of how "administer" is understood in the field of oncology and should be construed in the '209 patent; to the extent that the case law is helpful, it supports Lilly's position, not Defendants'.

4. The Product Labeling Induces Physicians to Administer Folic Acid

Besides the "single actor" rule and the parties' dispute regarding claim construction, Defendants also suggested at trial that there was no infringement because the labeling does not expressly require verifying that the patient has taken folic acid before giving pemetrexed, and therefore does not induce physicians to "administer" folic acid under Lilly's construction. This argument is wrong, not only because it ignores the evidence adduced at trial, but it also misapprehends the law of inducement.

As an initial matter, "verification" is not part of Lilly's construction, nor is it required to prove infringement. The evidence demonstrated that physicians carry out the steps the label requires of instructing patients to take folic acid and counseling them about the importance of their doing so, and that patients take folic acid in response to these instructions. Tr. 86, 97, 112, 132-34, 145, 174, 244-45. That is "administering" folic acid and thus literal infringement. The fact that, in reality, physicians may also take *additional* steps to verify patients' compliance with their instructions in order to ensure that their patients have in fact received the required folic acid does not make this verification a requirement of the claims. Tr. 86, 245. It is therefore

immaterial whether Defendants' label induces physicians to verify compliance or not.[6]

Moreover, contrary to Defendants' suggestion, even if verification were required by the claim, there is no requirement that the labeling must contain express instructions that physicians do this in order for the label to induce physicians to do so. Rather, the inquiry is whether the "proposed label . . . will *cause at least some* users to infringe the asserted method claims." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010) (emphasis added). Thus, even if "administering" required some verification beyond what the label expressly directs, the label still induces infringement so long as it causes at least one physician to carry out that verification. And the evidence showed that it does so; Dr. Chabner testified that the label induces physicians to verify that the patient has taken the folic acid, and that many physicians are induced by the label to go considerably further and to take additional steps such as counting pills or verifying patients' day-to-day pill diaries. Tr. 98-99, 112, 174. And Dr. Schulz asks each of his patients to verify that they have taken the vitamin B_{12}. Tr. 242-46. Accordingly, the label induces physicians to "administer" folic acid as that term is used in the '209 patent.

B. The Single Actor Rule Does Not Prohibit the Involvement of Someone Besides the Infringer

A principal focus of Defendants' argument and examinations at trial was on the fact that the patient, not the physician, physically swallows the folic acid pills. From this, Defendants suggested that the "single actor" rule could never be satisfied because there would always be action by the patient required in order for the requisite folic acid to get into the patient's body. Put another way, because administration of folic acid is not complete without the patient ingesting it, Defendants argue, there can be no infringement because no one party carries out the

[6] As will be discussed below, *see infra* Part III, the additional verification steps that the label induces physicians to take demonstrate physicians' direction and control over the treatment process, but they are not required for Lilly to demonstrate literal infringement.

entire claimed method. Tr. 46, 50-51.

Defendants wholly misapprehend the law of divided infringement. The question is not whether a second party is somehow "necessarily involved" in carrying out a patented method. *E.g.*, *Kenexa Brassring, Inc. v. Taleo Corp.*, 751 F. Supp. 2d 735, 751 (D. Del. 2010). Rather, the focus of the inquiry is on the *steps that the language of the claims specifically requires*—in this case, whether physicians carry out the step of "administering" folic acid. *Id.*; *Akamai Techs., Inc v. Limelight Networks, Inc.*, Nos. 2009-1372, et al., — F.3d —, 2015 WL 2216261, at *5 (Fed. Cir. May 13, 2015) (direct infringement requires that "all steps *of a method claim* are performed by or attributable to a single entity" (emphasis added)). Any antecedent, complementary, or subsequent steps that are not expressly set forth in the claim, whether performed by the same person or by a different person, are simply irrelevant to the question of whether a single actor has performed each of the steps that are *actually claimed*.

What Defendants are arguing goes beyond this rule and misstates what is legally required to prove infringement. That is, they seek to require that physicians not only take actions that meet the requirements of the claims for administration of folic acid, but that they do so *without any action by the patient*. *E.g.*, Tr. 59. The Federal Circuit has never articulated such a broad version of the "single actor" rule. To the contrary, both the Federal Circuit and the district courts have considered a number of cases in which one actor carried out each expressly claimed step, but a second party was also involved in some essential way. In each case, courts have found that there *was* infringement and that there had been no violation of the "single entity" rule.

For example, in *SiRF Technology, Inc. v. Int'l Trade Comm'n*, 601 F.3d 1319, 1331 (Fed. Cir. 2010), the Federal Circuit considered a method of updating handheld GPS receivers that a maker of GPS chips was alleged to infringe. The method at issue required "processing satellite

signals," and the accused maker of the GPS chips argued that there was no infringement under the "single actor" rule because no signals would be processed by its chips unless end users—i.e., someone other than the chip maker—first took the steps of enabling the GPS device and causing it to download particular data to be processed. *Id.* at 1329 & n.7, 1331 (internal quotation marks omitted). The Federal Circuit rejected this argument because "enabling" the device and "downloading" the data—though performed by someone besides the accused infringer and necessary for the claim to be carried out—were not expressly claimed steps of the method. *Id.* at 1331. There was thus no issue of divided infringement. So too here: even though the patient—*i.e.*, someone other than the physician—places the folic acid in her mouth and swallows it, it is the physician who administers the folic acid by directing that treatment and causing it to be received, and therefore it is the physician who performs the step which is expressly claimed.

Similarly, in *Ultratec, Inc. v. Sorenson Commc'ns, Inc.*, 45 F. Supp. 3d 881, 905 (W.D. Wis. 2014), the court considered a method of providing telecommunications to the deaf, requiring, among other steps, "transmitting the voice of the hearing person when speaking to the ear of the call assistant." *Id.* (internal quotation marks omitted). The defendant argued that it could not infringe because of the "single actor" rule: the defendant was the provider of the telecommunications service, not the "hearing person" referred to in the claim, and for the defendant to have anything to transmit, a second actor—the hearing person—had to speak. *Id.* The court disagreed, holding that the claimed step—"transmitting"—was performed by the accused infringer, and "speaking" was not a claimed step. *Id.* By analogy to this case, ingesting the folic acid has to happen here, but because it is not a claimed step, it is immaterial that it is performed by the patient rather than the doctor.

These cases are not outliers; time and again, courts have responded to "single actor"

arguments by focusing on the precise language of the claims and finding infringement where a single actor performed each claimed step, notwithstanding the required participation of a second actor for the claimed method to be carried out. *See Mortgage Grader, Inc. v. Costco Wholesale Corp.*, No. SACV13-00043AG(ANX), — F. Supp. 3d. —, 2015 WL 778125, at *15 (C.D. Cal. Jan. 12, 2015); *Kenexa*, 751 F. Supp. 2d at 750-51 (methods requiring "displaying" on a user's screen and "supplying" data originally entered by a user who was not the accused infringer).

In each of these cases, the dispositive question was whether the claimed steps were performed by one infringer, and the answer was that they were. The answer here is the same. The only claimed step is "administering," which, as the claim language emphasizes, refers to what physicians do "to a patient." *E.g.*, TX 1, claim 12. And as discussed above, a physician "administers" folic acid when she directs that the patient receive folic acid and causes that to occur. While a patient is necessarily involved in the method, and while the administration is not complete until the physician has actually caused that patient to receive the folic acid, it is the physician who performs the claimed step of "administering" folic acid to the patient, and thus there is a single actor—the physician—who practices the claim. *See SiRF*, 601 F.3d at 1331.

II. ALTERNATIVELY, PHYSICIANS WILL INFRINGE UNDER THE DOCTRINE OF EQUIVALENTS

Even if the Court adopts Defendants' proposed construction of "administer"—and, as a result, concludes that doctors will not literally infringe the '209 patent—Lilly is entitled to judgment of infringement under the doctrine of equivalents. That is because if they do not literally infringe, physicians perform a method that is "insubstantial[ly] differen[t]" from what is claimed. *Deere & Co. v. Bush Hog, LLC*, 703 F.3d 1349, 1356 (Fed. Cir. 2012).

Defendants argued at trial that the doctrine of equivalents should be unavailable as a matter of law because it would require a finding that "the conduct of two people [is] equivalent

to the conduct of one." Tr. 69. That is wrong. The question on the doctrine of equivalents is *not* whether the physician and patient, each "administering" part of the regimen, are equivalent to the physician "administering" alone. The question, rather, is whether the physician has performed "all of the claimed steps of the process . . . , either as claimed or by an equivalent step." *EMI Grp. N. Am., Inc. v. Intel Corp.*, 157 F.3d 887, 896 (Fed. Cir. 1998). That requires determining (1) what acts would literally infringe the claims, and then (2) analyzing whether what the physician actually does is equivalent to something within the literal scope of the claim.

Both sides agree that the doctor physically placing the folic acid pills into the patient's mouth would literally meet the folic acid administration limitation. The question, then, is whether the doctor's actual conduct is insubstantially different from placing folic acid pills in the patient's mouth.

The evidence showed that the actions that physicians take—and which Defendants' labeling induces them to take—are equivalent to physically putting the folic acid into the patients. Tr. 133-35. Per the label, physicians instruct their patients to take oral folic acid at dosages and on schedules that fall within Lilly's claims. Tr. 101-02. They also make clear to the patients the importance of taking the folic acid and that folic acid is required. Tr. 86, 111-12, 132-34, 240-43. There was no dispute that pemetrexed patients do in fact take the required folic acid as directed by their physicians, because they were directed to do so by their physician. Tr. 14, 68-69; *see also* Tr. 132-34. And both sides' experts agreed that when the patient does so, the folic acid works the same no matter who put it in the patient's mouth. Tr. 133-34, 254-55. Applying the "function-way-result" test—one way in which courts determine whether a step that a party performs is equivalent to a claimed step—the folic acid "performs substantially the same function in substantially the same way with substantially the same result" as the claimed step.

Brilliant Instruments, Inc. v. GuideTech, LLC, 707 F.3d 1342, 1347 (Fed. Cir. 2013) (internal quotation marks omitted). Instructing patients to take folic acid fulfills the same function (preventing toxicity) in the same way (providing a baseline folate level) with same result (the regimen is well-tolerated) as physically providing folic acid. Tr. 134. Accordingly, the doctor's actions are equivalent to an act that indisputably falls within the literal scope of the claims.

Defendants' factual response to this showing is Dr. Schulz's testimony that "the physician's instruction to take folic acid" is not equivalent to "the physician's actual administration of folic acid" because "mere instruction does not imply that the folic acid will be placed in the body." Tr. 221. The evidence was to the contrary. Both sides' experts agreed that they and other oncologists will not administer pemetrexed to a patient if the patient has not taken the required folic acid, meaning that in circumstances where Defendants' products will be used, the patient will have followed the doctor's instructions. Tr. 132-34, 243-45. Defendants tried to sow metaphysical doubt about whether patients who say they took the required folic acid (and who are told that they could die from pemetrexed if they don't take folic acid) in fact actually did take it. But there is no evidence of even one instance where anyone is aware of this actually happening, and there was no dispute that the vast majority of patients follow their physician's instructions. *Id*. Indeed, even in the face of possibly fatal side effects from failing to take folic acid, the FDA was willing to approve ALIMTA® with its existing labeling; thus, if there were more than an "insubstantial difference" between a doctor physically "administering" folic acid in Defendants' narrow sense of the term, and the regimen required by Lilly's (and Defendants') product labeling, then surely FDA would have required the ALIMTA® labeling to provide that doctors must physically administer folic acid.

In any event, the theoretical possibility that some cancer patient somewhere might lie to

their doctor is beside the point. The infringement inquiry hinges on whether Defendants induce *some* physicians to infringe, and thus (in the doctrine of equivalents context) on whether Defendants induce *some* physicians to take steps equivalent to physically administering folic acid. *AstraZeneca*, 633 F.3d at 1060; *Genentech, Inc. v. Trs. of Univ. of Pa.*, 871 F. Supp. 2d 963, 978 (N.D. Cal. 2012) ("[T]he Court need not find . . . infringement in every instance, so long as 'the language . . . would inevitably lead *some* consumers to practice the claimed method.'" (third alteration in original) (quoting *AstraZeneca*, 633 F.3d at 1060)). What matters is whether there are cases where patients do take folic acid as directed and whether those cases are equivalent to literal infringement. It does not matter whether there are *also* cases in which a patient lies. The evidence at trial showed that when the patients do take the folic acid, the way the claims are practiced is insubstantially different from the physician physically placing the folic acid in the patient's mouth; indeed, there is no material difference at all. Tr. 133, 254-55.

Defendants suggest that this result must be incorrect because it would "swallow the entire divided infringement rule." Tr. 70. Defendants are mistaken. Infringement by equivalents is available here because Lilly has shown that what the physician does in accordance with the labeling is insubstantially different from acts *of the physician* that would literally infringe the claim (assuming Defendants' construction is adopted), *i.e.*, physically putting folic acid into the patient's body. That will not be true in every case.[7]

Defendants also point to the statement in the most recent *Akamai* decision that

[7] For example, in *BMC Res., Inc. v. Paymentech, L.P.*, no one adduced evidence that the defendant performed steps equivalent to the ones performed by the other two actors (a payment network and a financial institution) or even raised the doctrine of equivalents. 498 F.3d 1373, 1381-82 (Fed. Cir. 2007). Similarly, in *Akamai*, the method required the defendant's customers to "tag[]" objects on a web page in a particular way, and then the defendant would respond to requests for those objects using its own computers. *Akamai Techs., Inc. v. Limelight Networks, Inc.*, 629 F.3d 1311, 1316-17 (Fed. Cir. 2010) (original, now-vacated panel opinion). There was no evidence that the defendant took any action that could be equivalent to "tagging." *Id*.

"[e]ncouraging or instructing others to perform an act is not the same as performing the act oneself," Tr. 71 (quoting *Akamai*, 2015 WL 2216261, at *1), and suggest that this forecloses showing equivalence based on instructing another to perform an act. Defendants ignore the context of that statement. The quote on which Defendants rely was about whether a service provider making instructions available to its customers was the same thing as the service provider actually performing the acts. That has nothing to do with the oncologist-patient context here, where the evidence overwhelmingly demonstrated that patients in fact follow their doctor's instructions (among other reasons, because their lives are at stake). Tr. 112-13, 132-34, 243-45. Moreover, *Akamai* had nothing to do with the doctrine of equivalents, which was not raised or discussed, and which *always* involves an act that is "not the same as" a literally infringing one. 2015 WL 2216261, at *1; *see Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 609 (1950). Simply put, *Akamai* does nothing to rebut the overwhelming evidence at trial that what Defendants' product labeling induces physicians to do is insubstantially different from physically putting the drug into the patient.

III. PHYSICIANS WILL DIRECT OR CONTROL THE ADMINISTRATION OF FOLIC ACID

Finally, Lilly is entitled to judgment on a third, independent ground: oncologists directly infringe Lilly's patent by exercising control or direction over the administration of folic acid as part of a pemetrexed regimen. As the Federal Circuit has emphasized, a party who "exercises 'control or direction' over the entire process" may be liable as a direct infringer even if they do not personally perform every step. *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318, 1329 (Fed. Cir. 2008) (citation omitted); *see BMC*, 498 F.3d at 1380.

Contrary to Defendants' assertion that control or direction is found *only* where there is an agency or contractual relationship, Tr. 64, these are "example[s]," and control or direction exists

wherever vicarious liability may attach. *See BMC*, 498 F.3d at 1379; *Akamai*, 2015 WL 2216261, at *6-7 ("[P]rinciples of vicarious liability govern § 271(a)" and "*include[], for example*, principal-agent relationships, contractual arrangements, and joint enterprises" (emphasis added)). The Supreme Court has also emphasized that vicarious liability is not so limited in the context of copyright law, which the Supreme Court has routinely analogized to patent law, *see, e.g.*, *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936-37 (2005); vicarious copyright liability is imposed in a wide variety of factual situations where one actor "was in a position to control the use of copyrighted works" and the imposition of such liability was "manifestly just." *Sony Corp. of Am. v. Universal City Studios, Inc.*, 464 U.S. 417, 437-38 (1984); *see id.* at 488 n.39 (Blackmun, J., dissenting) (collecting cases).

The common law also recognizes that physicians bear a special responsibility for the treatments they direct, and has therefore ascribed vicarious liability to physicians when their direction of a treatment leads to the commission of a tort. For example, while the common law ordinarily denies liability to "one who employs an independent contractor" who then engages in tortious conduct, physicians are liable for treatment errors made by individuals under their supervision, because the heightened risks to patients' health and life warrant imposition of a "nondelegable duty" on the physician. W. Page Keeton et al., *Prosser on Torts* § 33, at 204 & n.14 (5th ed. 1984) (citing Restatement (Second) of Torts § 409 (1965)); *see also Miller v. Ryan*, 706 N.E.2d 244, 251 (Ind. Ct. App. 1999) (physician having "dominion or control" is responsible for tasks delegated to another physician following his instruction). Likewise, courts have held physicians liable for patients' actions that result from following treatment instructions. *See, e.g.*, *Taylor v. Smith*, 892 So. 2d 887, 897 (Ala. 2004); *McCarroll v. Reed*, 679 P.2d 851, 852, 854 (Okla. Civ. App. 1983); *Argus v. Scheppegrell*, 472 So. 2d 573, 574 (La. 1985).

Considered in light of these principles of vicarious liability, the evidence at trial demonstrated that oncologists exercise control and direction over cancer chemotherapy such that they should be held liable for the infringing conduct that they cause. Oncologists determine and direct every step of the treatment. Tr. 98-99, 110-14, 133, 163-64, 173, 245-46. They place a specific order for each of the agents the patient is to receive, which they expect others to execute. And those others—whether a nurse or the patient—execute those orders on behalf of the physician, by infusing, injecting, or ingesting the agent as directed. Tr. 133, 136-38. As to folic acid, oncologists "sternly counsel" patients that failure to comply with their orders is life-threateningly dangerous, to the extent that they withhold the life-saving chemotherapy if the patient fails to comply. Tr. 163, 245. They also use a variety of verification and enforcement mechanisms to ensure that their orders are followed, which vary from having patients sign consent forms to counting pills to having patients keep pill diaries, to ensure the patient takes folic acid as instructed. *See* Tr. 96-99, 163, 241-43, 245. And they exercise this control, and are responsible for the treatment, in a context that is literally life-and-death. Tr. 113.[8]

In contrast, the cases on which Defendants rely, in which the Federal Circuit has rejected claims that one party exercises direction or control over another, were in the context of claims to

[8] Defendants suggested that there is a lack of control because the Patient Prescribing Information, TX 3017, "leaves a lot of decisions up to the patient," Tr. 44—in particular, they contend that patients are free to choose a folic acid dosage between 400 and 1000 µg. That is not right; Dr. Chabner testified that most physicians in fact prescribe a specific dosage. But even if it were, it is completely beside the point because whatever dosage the patients may take between 400 and 1000 µg, the doctor has caused them to practice the claims, which require administration of "between about 350 µg and 1000 µg of folic acid," TX 1, claim 12. The same is true for any limited flexibility patients have as to when to take folic acid (and specific timing is in any event a limitation of only one asserted claim, TX 1 claim 19). The possibility that patients have some flexibility to choose a dose and schedule within the requirements of the claim (or indeed to control some other unrelated parameter such as where they buy the pills or whether they take them in the bathroom or the kitchen) is immaterial.

the use of a computer system.[9] The absence of direction or control in that setting has no bearing here because oncologists exercise close supervision over pemetrexed treatment that has no parallel in the context of computer software patents. Tr. 96-99, 112-13, 132-34, 163, 241-45. A customer who fails to follow the instructions on a web site will, at worst, fail to succeed in using the web site for its intended purpose. A patient who fails to abide by his oncologist's orders risks severe, possibly life-threatening toxicity.

Under these circumstances, it is fully appropriate for the oncologist to be held vicariously liable for specific acts that the oncologist causes, including patients' ingestion of folic acid. *See* Prosser § 33. And because oncologists are vicariously liable, Defendants infringe the '209 patent under *Akamai*. 2015 WL 2216261, at *6.

CONCLUSION

For the reasons discussed above, at trial, and in Lilly's pre-trial brief, Lilly has demonstrated by a preponderance of the evidence that Defendants will be liable for inducing and contributing to infringement of the '209 patent.

Respectfully submitted,

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[9] *See Akamai*, 2015 WL 2216261 (electronic content delivery network); *BMC*, 498 F.3d 1373 (electronic bill pay); *Muniauction,* 532 F.3d 1318 (bidding software); *McKesson Techs., Inc. v. Epic Sys. Corp.*, No. 2010-1291, 2011 U.S. App. LEXIS 7531 (Fed. Cir. April 12, 2011), *vacated,* 463 F. App'x 906 (Fed. Cir. 2011) (healthcare software); *Voter Verified, Inc. v. Premier Election Solutions, Inc.*, 698 F.3d 1374 (Fed. Cir. 2012) (voting software); *Move, Inc. v. Real Estate Alliance Ltd.*, 709 F.3d 1117, 1119 (Fed. Cir. 2013) (real estate software); *Emtel, Inc. v. Lipidlabs, Inc.*, 583 F. Supp. 2d 811 (S.D. Tex. 2008) (videoconferencing networks).

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